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Tami M. Procopio
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:

Jeffrey J. Seilhamer, *et al.*

Serial No.: Divisional of 09/287,892

Filing Date: Even Date Herewith

For: RECOMBINANT TECHNIQUES FOR
PRODUCTION OF BRAIN
NATRIURETIC PEPTIDE

Examiner: Not Assigned

Group Art Unit: Not Assigned

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Prior to examination of the application herein, please amend the specification as follows:

Please amend the title to read --IMMUNOASSAYS FOR HUMAN AND CANINE
BRAIN NATRIURETIC PEPTIDE--

On page 1 of the specification, please delete the paragraph set forth under "Cross-
Reference to Related Application" and substitute therefor

--This application is a divisional of U.S. Serial No. 09/287,892 filed 7 April 1999 which
is a divisional of U.S. Serial No. 08/850,910 filed 5 May 1997 and now U.S. patent 5,948,761
which is a continuation of U.S. Serial No. 07/477,226 filed 8 February 1990 and now U.S. patent
5,674,740 which is a divisional application of U.S. Serial No. 07/299,880 filed 19 January 1989,

now abandoned which is a continuation-in-part of U.S. Serial No. 07/206,470 filed 14 June 1988 and now abandoned which is a continuation-in-part of U.S. Serial No. 07/200,383 filed 31 May 1988 and now abandoned. Also related is U.S. Serial No. 07/460,855, now patent No. 5,114,923 which is a continuation-in-part of U.S. Serial No. 07/299,880 listed above.--

Please amend the claims as follows:

Please cancel claims 1-31 and substitute the following claims:

--32. Antibodies useful for immunoassays to detect a peptide which peptide comprises human or canine brain natriuretic peptide.

33. The antibodies of claim 32 wherein said peptide is human brain natriuretic peptide of the formula:

R^1 -Cys-Phe-Gly-Arg-Lys-Met-Asp-Arg-Ile-Ser-Ser-Ser-Ser-Gly-Leu-Gly-Cys- R^2

wherein R^1 is selected from the group consisting of:

(H);

Gly-;

Ser-Gly-;

Gly-Ser-Gly-;

Gln-Gly-Ser-Gly-;

Val-Gln-Gly-Ser-Gly-;

Met-Val-Gln-Gly-Ser-Gly-;

Lys-Met-Val-Gln-Gly-Ser-Gly-;

Pro-Lys-Met-Val-Gln-Gly-Ser-Gly-;

Ser-Pro-Lys-Met-Val-Gln-Gly-Ser-Gly-; and

R^3 -Ser-Pro-Lys-Met-Val-Gln-Gly-Ser-Gly-

wherein R^3 is the 101 amino acid sequence shown for human BNP in Figure 8 at positions numbered 1-99 immediately upstream of the Ser residue to which R^3 is bound, or a C-terminal portion thereof; and

R^2 is OH, NH_2 or NR_2 wherein each R is independently H or lower alkyl (1-4C); or R^2 is selected from the group consisting of:

Lys;
Lys-Val;
Lys-Val-Leu;
Lys-Val-Leu-Arg;
Lys-Val-Leu-Arg-Arg; and
Lys-Val-Leu-Arg-Arg-His, or
the C-terminal amides thereof.

34. The antibodies of claim 33 wherein the peptide is of the formula:

Ser-Pro-Lys-Met-Val-Gln-Gly-Ser-Gly-Cys-Phe-Gly-Arg-Lys-Met-Asp-Arg-Ile-Ser-Ser-Ser-Ser-Gly-Leu-Gly-Cys-Lys-Val-Leu-Arg-Arg-His,
or a C-terminal amide thereof.

35. The antibodies of claim 33 wherein, in said human brain natriuretic peptide, R^3 is H and R^2 is OH or NH_2 .

36. The antibodies of claim 33 wherein, in said human brain natriuretic peptide, R^1 is H and R^2 is OH or NH_2 .

37. The antibodies of claim 32 wherein said peptide is canine natriuretic peptide of the formula:

R^1 -Cys-Phe-Gly-Arg-Arg-Leu-Asp-Arg-Ile-Gly-Ser-Leu-Ser-Gly-Leu-Gly-Cys- R^2
wherein R^1 is selected from the group consisting of:

(H);
Gly-;
Ser-Gly-;
Lys-Ser-Gly-;
His-Lys-Ser-Gly-;
Met-His-Lys-Ser-Gly-;

Met-Met-His-Lys-Ser-Gly-;
Lys-Met-Met-His-Lys-Ser-Gly-;
Pro-Lys-Met-Met-His-Lys-Ser-Gly-; and
R³-Ser-Pro-Lys-Met-Met-His-Lys-Ser-Gly-;

wherein R³ is the 100 amino acid sequence of the dog prepro sequence upstream of the Ser residue to which R³ is bound shown in Figure 8 herein or a C-terminal portion thereof;

R² is OH, NH₂, or NR₂ wherein each R is independently H or lower alkyl (1-4C) or R² is

Asn;

Asn-Val;

Asn-Val-Leu;

Asn-Val-Leu-Arg;

Asn-Val-Leu-Arg-Lys; or

Asn-Val-Leu-Arg-Lys-Tyr;

or a C-terminal amide thereof.

38. The antibodies of claim 37 wherein said canine natriuretic peptide is
Ser-Pro-Lys-Met-Met-His-Lys-Ser-Gly-Cys-Phe-Gly-Arg-Arg-Leu-Asp-Arg-Ile-Gly-
Ser-Leu-Ser-Gly-Leu-Gly-Cys-Ser-Pro-Lys-Met-Met-His-Lys-Ser-Gly-Asn-Val-Leu-
Arg-Lys-Tyr;
or a C-terminal amide thereof.

39. The antibodies of claim 37 wherein the said canine natriuretic peptide R³ is H and
R² is OH or NH₂.

40. The antibodies of claim 37 wherein the said canine natriuretic peptide R¹ is H and
R² is OH or NH₂.

41. The antibodies of claim 32 which are monoclonal antibodies.

42. The antibodies of claim 32 which further comprise a label.

43. A method to perform an immunoassay to detect human or canine brain natriuretic peptide in a sample which method comprises contacting said sample with the antibodies of claim 32 and assessing the ability of said antibodies to immunoreact with one or more components contained in said sample.

44. A kit for conducting an immunoassay to detect human or canine brain natriuretic peptide which kit comprises the antibodies of claim 32 in containers and reagents capable of recognizing and specifically binding to said peptides or said antibodies in additional containers.

REMARKS

This application is a divisional filed to claim subject matter set forth on pages 35-36 of the specification. As noted, beginning at line 24, the peptides claimed herein can be used to prepare antibodies which may be monoclonal (see page 36, line 6). These antibodies are useful in immunoassays to detect the peptides and thus in kits designed for performing such immunoassays. No new matter has been added and entry of the amendment is respectfully requested.

It will be noted that claims to the peptides themselves have been granted and are issued in U.S. patent 5,948,761 and U.S. patent 5,114,923; claims to the recombinant materials related to the human peptides are granted in U.S. patent 5,674,710.

Attached hereto is a final version of the changed paragraphs made to the specification; and all the claims according to the current amendment. The attached page is captioned "**Version as Amended**".

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 219002025213. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: July 9, 2001

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VERSION AS AMENDED

In the Specification:

[RECOMBINANT TECHNIQUES FOR PRODUCTION OF BRAIN NATRIURETIC PEPTIDE]

--IMMUNOASSAYS FOR HUMAN AND CANINE BRAIN NATRIURETIC PEPTIDE--

[Cross-Reference to Related Application

This is a continuation-in-part of U.S. Serial No. 206,470, filed 14 June 1988, which is a continuation-in-part of U.S. Serial No. 200,383, filed 31 May 1988.]

--Cross-Reference to Related Application

This application is a divisional of U.S. Serial No. 09/287,892 filed 7 April 1999 which is a divisional of U.S. Serial No. 08/850,910 filed 5 May 1997 and now U.S. patent 5,948,761 which is a continuation of U.S. Serial No. 07/477,226 filed 8 February 1990 and now U.S. patent 5,674,740 which is a divisional application of U.S. Serial No. 07/299,880 filed 19 January 1989, now abandoned which is a continuation-in-part of U.S. Serial No. 07/206,470 filed 14 June 1988 and now abandoned which is a continuation-in-part of U.S. Serial No. 07/200,383 filed 31 May 1988 and now abandoned. Also related is U.S. Serial No. 07/460,855, now patent No. 5,114,923 which is a continuation-in-part of U.S. Serial No. 07/299,880 listed above.--